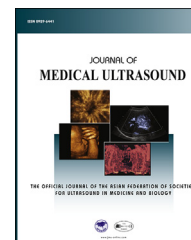




Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jmu-online.com



ORIGINAL ARTICLE

Submental Ultrasonography in Diagnosing Severe Obstructive Sleep Apnea Syndrome



Li-Jen Liao^{1,2}, Tsung-Yi Cho¹, Po-Wen Cheng¹, Chi-Te Wang¹,
Wu-Chia Lo¹, Tsung-Wei Huang^{1,2,3*}

¹ Department of Otolaryngology, Far Eastern Memorial Hospital, Taipei, ² Department of Electrical Engineering, Yuan Ze University, Taoyuan, and ³ Department of Health Care Administration, Oriental Institute of Technology, Taipei, Taiwan

Received 26 April 2016; accepted 17 June 2016

Available online 18 August 2016

KEYWORDS

obstructive,
sleep apnea,
sleep disorders,
ultrasound

Abstract *Background:* The aim of this study was to compare multiple ultrasound parameters in diagnosing patients with severe obstructive sleep apnea syndrome (OSAS).

Methods: A submental ultrasonography was performed to measure the distance between the lingual arteries, the diameter of the retropalatal space in the transverse dimension, and the tongue base thickness in the sagittal plane. The diameter of the retropalatal space and tongue base thickness were measured in the resting state and under Müller's maneuver. Analyses were based on the means of the triplicate measurements and the severity of OSAS.

Results: Based on ultrasound data, patients with severe OSAS had a significantly larger mean tongue base thickness in the resting state and under Müller's maneuver and a larger mean distance between the lingual arteries. The mean tongue base thickness (≥ 60 mm, odds ratio 5.18; 1.07–25.0) is the sole independent predictor for severe OSAS. The resting tongue base thickness (≥ 60 mm) had a diagnostic performance of 84.9% sensitivity, 59.3% specificity, 75.0% positive predictive value, 72.7% negative predictive value, and 74.2% accuracy for severe OSAS.

Conclusion: Submental ultrasonography is a noninvasive, convenient, and effective tool in diagnosing severe OSAS.

© 2016, Elsevier Taiwan LLC and the Chinese Taipei Society of Ultrasound in Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Conflict of interest: The authors declare that they have no conflicts of interest relevant to this article.

* Correspondence to: Dr Tsung-Wei Huang, Department of Otolaryngology, Far Eastern Memorial Hospital, Number 21, Section 2, Nan-Ya South Road Pan Chiao, Taipei 220, Taiwan.

E-mail address: huangtw28@gmail.com (T.-W. Huang).

<http://dx.doi.org/10.1016/j.jmu.2016.06.002>

0929-6441/© 2016, Elsevier Taiwan LLC and the Chinese Taipei Society of Ultrasound in Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Sleep-disordered breathing is becoming more common and it is related to increased morbidity and mortality in the general population [1]. According to previous literature reports, 9% of women and 24% of men have sleep-disordered breathing [2].

Obstructive sleep apnea syndrome (OSAS) is independently associated with increased carotid intima-media thickness and plaque, which could increase future cardiovascular disease risk [3–5].

The management of OSAS is not easy to assess. It involves specialist referrals, and the diagnosis and grading of OSAS depends on polysomnography data that can only be

collected after an overnight examination [6]. When the Apnea–Hypopnea Index (AHI) or Respiratory Disturbance Index contains >30 events/h, it is classified as severe OSAS [7]. Severe OSAS increases the risk of cardiovascular disease, and it is indicative of the need for further treatment. Surgical treatment or positive pressure during sleep can decrease the AHI, minimum and mean oxygen saturation, blood pressure, and carotid intima-media thickness, which can attenuate the risk of morbidity and mortality [8–10].

Due to the convenience, inexpensiveness, non-irradiation, and office-based procedure, an increasing number of ear, nose, and throat specialists use ultrasonography (US) to examine the neck [11]. US has been most

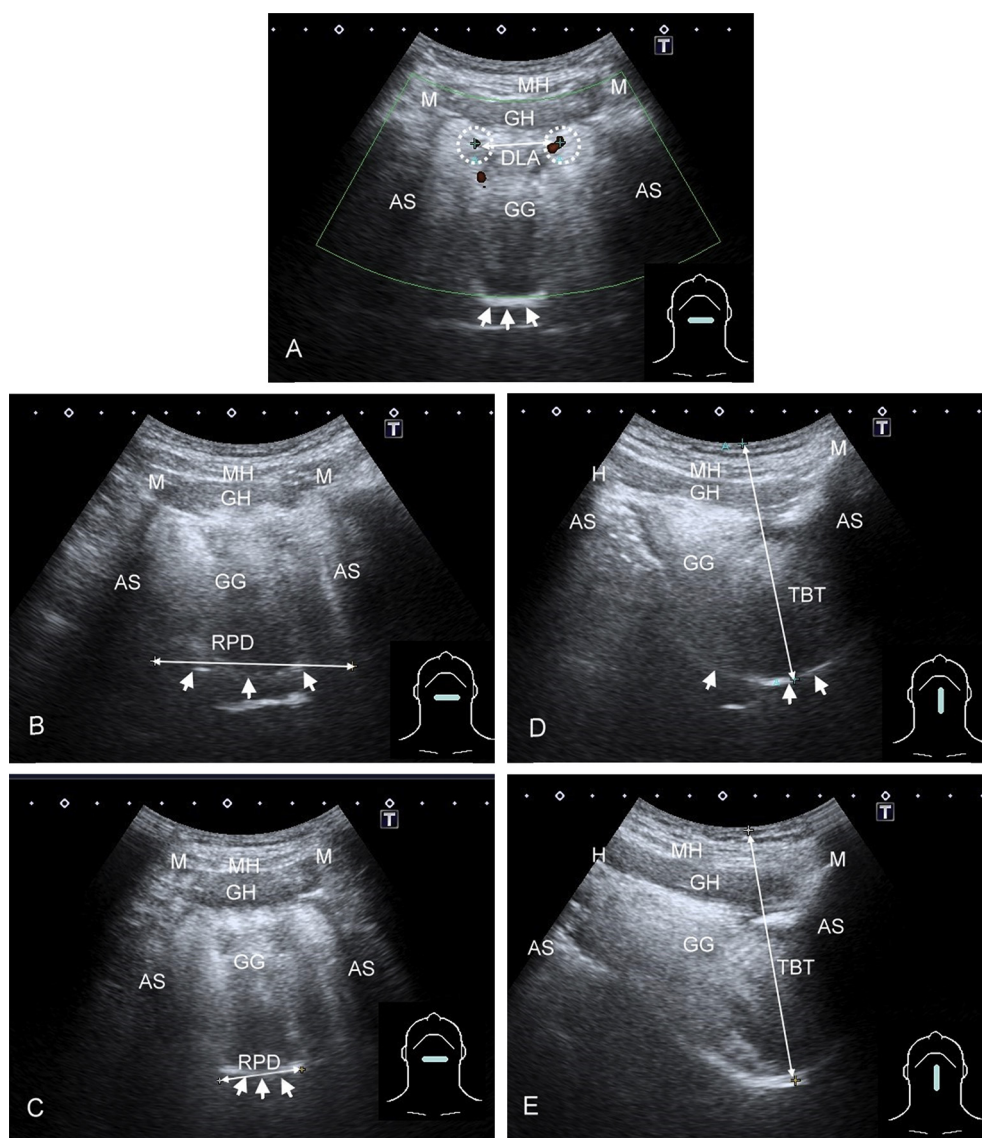


Figure 1 Submental ultrasonograms to delineate various ultrasound parameters in diagnosing severe obstructive sleep apnea syndrome. (A) Lingual arteries (dotted circles) were shown by Power Doppler scan on both sides of lower lateral border of tongue base. Distance between lingual arteries (DLA) was measured; (B) transverse diameter of rectropalatal pharynx (RPD) in resting and (C) under Müller's maneuver; (D) mid-tongue base thickness (TBT) in resting and (E) under Müller's maneuver. Other markings were seen as following: mucosa covering of tongue (whitish arrows), and geniohyoid muscle (GH), mylohyoid muscle (MH), geniohyoid muscle (GG), and acoustic shadow (AS) reflecting the mandible body (M) or hyoid bone (H).

frequently used to examine neck lumps, such as thyroid nodules, lymphadenopathy, or salivary gland tumors [12–16]. US can also guide fine-needle aspiration or core-needle biopsy for neck masses [17]. For sleep disorder patients, US has been used to evaluate the carotid intima-media thickness and level of obstruction in recent years [3,4,8,18–20]. Lahav et al [15] first used a tongue base US to measure the width of the tongue base, and demonstrated the possible role of US in diagnosing OSAS. Shu et al [19] used the retropharyngeal diameter to determine the severity of OSAS, and proposed a prediction model. Chen et al [20] verified the tongue base thickness, which also provides a quantitative assessment of the retroglossal airway. These reports show a promising role for US in diagnosing OSAS.

Although these US parameters were previously reported for sleep disorder evaluation, no external validation has been conducted. The aim of this study was to validate multiple US parameters in evaluating OSAS patients.

Material and methods

Patients and US

This was a prospective study which was approved by an Institutional Review Board (103066-E) and informed consent was obtained from all patients. Patients came to our clinic with a main complaint of snoring, and they received an overnight polysomnography examination and neck US. Demographic data and the Epworth sleepiness score was assessed and recorded. Submental US was performed by a head and neck surgeon who is experienced in neck US. The patients were scanned with a Toshiba Aplio 500 Platinum platform (Otaward, Japan) using a 1–6-MHz convex transducer. We conducted triplicate measurements of the distance between lingual arteries (DLA), the diameter of retropalatal space (RPD) in the transverse dimension, and tongue base thickness in the sagittal plane (Figures 1A–E). The scanning was carried out according to previous reports [18–20]. Analyses were based on the means of the three measurements. The RPD and tongue base thickness were measured during the resting state and under Müller's maneuver. The definition of severe OSAS was Respiratory Disturbance Index ≥ 30 .

Statistical analysis

Continuous data were expressed as the mean \pm standard deviation. Categorical data were expressed as a number and percentage. Means were compared using an unpaired Student *t* test, and categorical data were compared with the Pearson's Chi-square test. The association between predictors and severe OSAS was analyzed using the receiver operating characteristic curve method. An optimal cutoff point was determined at the point of greatest "sensitivity" with the corresponding smallest "1-specificity" [21]. A logistic regression was further used to test significant ultrasonographic predictors for severe OSAS. A value of $p < 0.05$ was accepted as statistically significant. All statistical analyses were accomplished

using Stata software, version 12.0 (Stata Corp LP, College Station, TX, USA).

Results

From January 2015 to January 2016, a total of 66 patients with the main complaint of snoring and suspected to have OSAS were enrolled, including nine women and 57 men. Their ages ranged from 20 years to 67 years with a mean of 42.8 ± 11.7 years. Body height ranged from 150 cm to 187 cm with a mean of 168.6 ± 8.1 cm. Weight ranged from 43 kg to 124 kg with a mean of 78.5 ± 15.6 kg. Body mass index ranged from 17.9 kg/m^2 to 40.1 kg/m^2 with a mean of $27.5 \pm 4.7 \text{ kg/m}^2$. Neck circumference ranged from 28 cm to 52 cm with a mean of 40.8 ± 4.7 cm. Epworth sleepiness score ranged from 0 to 21 with a mean of 8.9 ± 4.3 . AHI ranged from 1.9 to 96.8 with a mean of 43.2 ± 26.7 ; 39 cases were classified as severe OSAS with AHI ≥ 30 .

We further classified the severity of the sleep disorder according to whether the value of AHI was ≥ 30 and did further analysis. The demographic data and US parameters are shown in Table 1. People with severe OSAS had significantly higher body weight (mean 84.92 vs. 69.54 kg, $p < 0.01$) and BMI (mean 24.57 vs. 29.65 kg/m^2 , $p < 0.01$). Based on US data, people with severe OSAS had a significantly larger mean resting tongue base thickness (mean 65.9 vs. 59.8 cm, $p < 0.01$), mean tongue base thickness under Müller's maneuver (mean 64.9 vs. 59.5 cm, $p = 0.01$), and DLA (mean 33.0 vs. 27.9 cm, $p = 0.01$). However, the mean RPD (mean 61.7 vs. 51.8 cm, $p = 0.06$) and mean RPD under Müller's maneuver (mean 52.0 vs. 51.8 cm, $p = 0.93$) were not significantly different between these two groups. For severe OSAS patients, the mean Epworth sleepiness score was more serious (mean 9.74 vs. 7.59, $p = 0.046$).

Receiver operating characteristic curve analysis was used to determine the significant US predictors for severe OSAS that are listed in Table 1. The results are shown in Table 2 and Figure 2. The area under the receiver operating characteristic curve for the mean resting tongue base thickness, Müller's tongue base thickness, and DLA were 0.74 (95% confidence interval: 0.61–0.87), 0.68 (0.55–0.80), and 0.69 (0.55–0.83), respectively (all $p < 0.05$). The best cutoff point for mean resting tongue base thickness was 60 mm with 84.9% sensitivity, 59.3% specificity, 75.0% positive predictive value (PPV), 72.7% negative predictive value (NPV), and 74.2% overall accuracy. The best cutoff point for mean tongue base thickness in Müller's maneuver was 63.5 mm with 59.0 % sensitivity, 77.8 % specificity, 79.3% PPV, 56.8% NPV, and 66.7 % overall accuracy. The best cutoff point for mean DLA was 30 mm with 66.7% sensitivity, 59.3% specificity, 70.3% PPV, 55.2% NPV, and 63.6% overall accuracy, respectively.

The results of logistic regression are shown in Table 3. Based on the univariate logistic regression data, the mean resting tongue base thickness (≥ 60 mm, odds ratio (OR) 8.0; 95% confidence interval 2.5–25.2), the mean tongue base thickness in Müller's maneuver (≥ 63.5 mm, OR 5.0; 1.7–15.2), and the mean DLA (≥ 30 mm, OR 2.91; 1.05–8.0) were significant predictors of severe OSAS. After

Table 1 Patients were classified as Apnea–Hypopnea Index ≥ 30 (severe obstructive sleep apnea syndrome) or <30 according to the results from an overnight polysomnography exam.

	<30 (27)	≥ 30 (39)	<i>p</i>
Age	39.86	44.77	0.095
Sex (M/F)	21/6	36/3	0.091
Body height (cm)	167.94	169.05	0.593
Body weight (kg)	69.54	84.92	0.000
Body mass index (kg/m ²)	24.57	29.65	0.000
NC (cm)	38.08	42.7	0.000
Alcohol drinking	2	8	0.144
Cigarette smoking	6	12	0.443
Blood type (A/B/AB/O)	9/3/3/9	10/12/1/15	0.136
Ultrasonographic findings			
RPD (mm)	57.84	61.73	0.054
Müller's RPD (mm)	51.81	52.02	0.930
Resting tongue base thickness (mm)	59.84	65.91	0.001
Müller's tongue base thickness (mm)	59.53	64.94	0.010
DLA (mm)	27.94	32.96	0.012
Hypertension	4/27	15/39	0.037
Diabetes mellitus	1/27	7/39	0.081
Epworth sleepiness score	7.59	9.74	0.046

DLA = distance between lingual arteries; F = female; M = male; NC = neck circumference; RPD = retropalatal diameter.

Table 2 Receiver operating characteristic curve analysis for best cutoff point in significant ultrasound predictors for severe obstructive sleep apnea syndrome.

	Sen. (%)	Spe. (%)	PPV (%)	NPV (%)	Accuracy (%)
Resting tongue base thickness (60 mm)	84.6	59.3	75.0	72.7	74.2
Müller's tongue base thickness (63.5 mm)	59.0	77.8	79.3	56.8	66.7
DLA (30 mm)	66.7	59.3	70.3	55.2	63.64

DLA = distance between lingual arteries; NPV = negative predictive value; PPV = positive predictive value; Sen. = sensitivity; Spe. = specificity.

Table 3 Univariate and multivariate logistic regression for analysis of significant ultrasound predictors in severe obstructive sleep apnea syndrome.

	Univariate odds ratio	95% CI	<i>p</i>	Multivariate odds ratio	95% CI	<i>p</i>
Age (y)	1.04	0.99–1.09	0.097	1.01	0.95–1.06	0.805
Sex (M/F)	3.43	0.78–15.16	0.104	0.83	0.12–5.74	0.851
Resting tongue base thickness (≥ 60 mm)	8.00	2.51–25.52	0.000	5.18	1.07–24.96	0.041
Müller's tongue base thickness (≥ 63.5 mm)	5.03	1.66–15.25	0.004	1.92	0.49–7.57	0.350
DLA (≥ 30 mm)	2.91	1.05–8.04	0.039	2.05	0.63–6.68	0.236

CI = confidence interval; DLA: distance between lingual arteries; F = female; M = male.

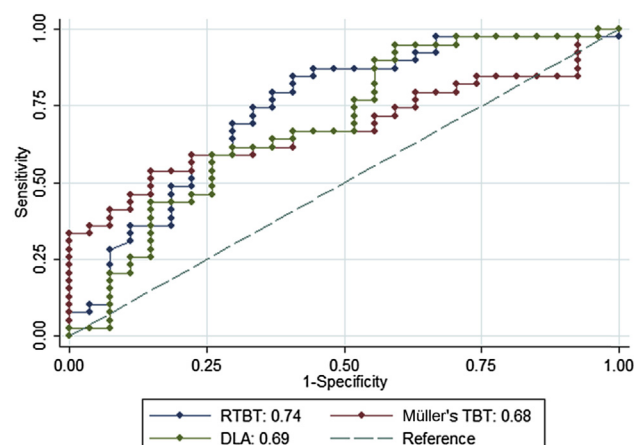


Figure 2 Receiver operator characteristic curve analysis of significant ultrasound predictors for severe obstructive sleep apnea syndrome. The area under the receiver operator characteristic curve for mean resting tongue base thickness (TBT), Müller's TBT, and DLA were 0.74 (95% confidence interval: 0.61–0.87), 0.68 (0.55–0.80), and 0.69 (0.55–0.83), respectively.

multivariate logistic regression, the mean resting tongue base thickness (≥ 60 mm, OR 5.18; 1.07–25.0) was the sole independent predictor for severe OSAS.

Discussion

Our results support the hypothesis that ultrasonic tongue base thickness is an independent predictor for severe OSAS. With the cutoff point as 60 mm, submental US has 84.9% sensitivity, 59.3% specificity, 75.0% PPV, 72.7% NPV, and 74.2% overall accuracy to diagnose severe OSAS. An US measurement of the tongue base thickness provides an effective assessment of the retroglottal airway in sleep-related disorders with minimal invasiveness and easy accessibility.

Lahav et al [18] first used US to determine the width of the tongue base for sleep disorder breathing patients. They concluded that when DLA exceeded 30 mm, the risk of moderate to severe OSAS increased significantly. Our results show that with the cutoff point of 30 mm for DLA, the sensitivity, specificity, PPV, NPV, and accuracy were 66.7%,

59.3%, 70.3%, 55.2%, and 63.6%, respectively. The DLA could be correlated with the width of tongue base and reflect the severity of OSAS. The lingual arteries are superficial to the retropalatal space and they are easier to assess.

Shu et al [19] reported that a change of Müller's RPD was an independent predictor of severe OSAS, and they proposed a prediction model combined with neck circumference and a decreased proportion of Müller's RPD. In our study, the RPD and reduced proportion of Müller's RPD were not different for these two groups. In our experience, the image of retropharyngeal space was difficult to capture with the currently used US probe. Cheng et al [20] reported that tongue base thickness could be an important anatomic factor in airway narrowing in patients with OSAS, and he emphasized the dynamic change under Müller's maneuver. In our study, with a cutoff point of 60 mm, the tongue base thickness had a better diagnostic performance to diagnose severe OSAS. However, in our study, the tongue base thickness under Müller's maneuver had some variations; some patients had elongated but others displayed shortened tongue base thickness. After logistic regression, the tongue base thickness (≥ 60 mm) was the sole independent predictor for severe OSAS. For consistency and feasibility, we suggest using the tongue base thickness parameter (≥ 60 mm) to screen for severe OSAS.

Moreover, patients with OSAS also had a higher proportion of hypertension that could increase their risk of cardiovascular disease (Table 1). These results highlight the importance of intervention for these patients. In one recent report, surgery for OSAS was demonstrated to improve the AHI, minimum and mean oxygen saturation, blood pressure, triglyceride, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol, which can also decrease carotid intima-media thickness [8].

Our study has some limitations: firstly, the number of recruited patients was limited. Secondly, the patients were awake during the exam; therefore, they did not fully mimic their sleeping condition. Furthermore, a sleep-induced US could be more potent for the evaluation of OSAS patients. Thirdly, the obstructive level was varied, but we only analyzed the retroglossal level. We did not routinely use acoustic rhinomanometry for these patients; therefore, nasal airway obstruction was not recorded. Fourthly, the treatment effect of OSAS was not followed by an US; thus, the difference in these US parameters need to be evaluated in the future.

In conclusion, submental US is a safe, convenient, and effective tool in diagnosing OSAS.

Acknowledgments

This work was supported by grants from the Far Eastern Memorial Hospital (FEMH-2015-C-038).

References

- [1] Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med* 2009;6:e1000132.
- [2] Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 2002;165:1217–39.
- [3] Gunnarsson SI, Peppard PE, Korcarz CE, et al. Obstructive sleep apnea is associated with future subclinical carotid artery disease: thirteen-year follow-up from the Wisconsin sleep cohort. *Arterioscler Thromb Vasc Biol* 2014;34:2338–42.
- [4] Nadeem R, Harvey M, Singh M, et al. Patients with obstructive sleep apnea display increased carotid intima media: a meta-analysis. *Int J Vasc Med* 2013;2013:839582.
- [5] O'Leary DH, Polak JF, Kronmal RA, et al. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. *Cardiovascular Health Study Collaborative Research Group. N Engl J Med* 1999;340:14–22.
- [6] Mansfield DR, Antic NA, McEvoy RD. How to assess, diagnose, refer and treat adult obstructive sleep apnoea: a commentary on the choices. *Med J Aust* 2013;199:S21–6.
- [7] Tsara V, Amfilochiou A, Papagrigoriakis MJ, et al. Guidelines for diagnosis and treatment of sleep-related breathing disorders in adults and children. Definition and classification of sleep related breathing disorders in adults: different types and indications for sleep studies (Part 1). *Hippokratia* 2009;13:187–91.
- [8] Peng Y, Zhang L, Hu D, et al. Reduction of internal carotid artery intima-media thickness in patients with moderate-to-severe obstructive sleep apnea syndrome after nasal surgery and uvulopalatopharyngoplasty. *Acta Otolaryngol* 2016;1–8.
- [9] Bliwise DL, Bliwise NG, Partinen M, et al. Sleep apnea and mortality in an aged cohort. *Am J Public Health* 1988;78:544–7.
- [10] Keenan SP, Burt H, Ryan CF, et al. Long-term survival of patients with obstructive sleep apnea treated by uvulopalatopharyngoplasty or nasal CPAP. *Chest* 1994;105:155–9.
- [11] Costache A, Dumitru M, Anghel I, et al. Ultrasonographic anatomy of head and neck—a pictorial for the ENT specialist. *Med Ultrason* 2015;17:104–8.
- [12] Cheng PW, Chou HW, Wang CT, et al. Evaluation and development of a real-time predictive model for ultrasound investigation of malignant thyroid nodules. *Eur Arch Otorhinolaryngol* 2014;271:1199–206.
- [13] Liao LJ, Wang CT, Young YH, et al. Real-time and computerized sonographic scoring system for predicting malignant cervical lymphadenopathy. *Head Neck* 2010;32:594–8.
- [14] Lo WC, Chang WC, Lin YC, et al. Ultrasonographic differentiation between Kikuchi's disease and lymphoma in patients with cervical lymphadenopathy. *Eur J Radiol* 2012;81:1817–20.
- [15] Lo WC, Cheng PW, Wang CT, et al. Real-time ultrasound elastography: an assessment of enlarged cervical lymph nodes. *Eur Radiol* 2013;23:2351–7.
- [16] Lo WC, Cheng PW, Wang CT, et al. Pain levels associated with ultrasound-guided fine-needle aspiration biopsy for neck masses. *Head Neck* 2014;36:252–6.
- [17] Ahn D, Sohn JH, Yeo CK, et al. Feasibility of surgeon-performed ultrasound-guided core needle biopsy in the thyroid and lymph nodes. *Head Neck* 2016;38:E1413–8.
- [18] Lahav Y, Rosenzweig E, Heyman Z, et al. Tongue base ultrasound: a diagnostic tool for predicting obstructive sleep apnea. *Ann Otol Rhinol Laryngol* 2009;118:179–84.
- [19] Shu CC, Lee P, Lin JW, et al. The use of sub-mental ultrasonography for identifying patients with severe obstructive sleep apnea. *PLoS One* 2013;8:e62848.
- [20] Chen JW, Chang CH, Wang SJ, et al. Submental ultrasound measurement of dynamic tongue base thickness in patients with obstructive sleep apnea. *Ultrasound Med Biol* 2014;40:2590–8.
- [21] Akobeng AK. Understanding diagnostic tests 3: receiver operating characteristic curves. *Acta Paediatr* 2007;96:644–7.